



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-0785]

General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drugs Products; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products." This draft guidance recommends studies, including comparative in vitro studies, which should be conducted to demonstrate that a proposed generic solid oral opioid drug product is no less abuse-deterrent than its reference listed drug.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to

<http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2016-D-0785 for "General Principles for Evaluating the Abuse-Deterrence of Generic Solid Oral Opioid Drugs." Received comments will be placed in the docket and, except for those submitted as

"Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the

prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Gail Schmerfeld, Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-9291, email: gail.schmerfeld@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products." Prescription opioid analgesics are an important component of modern pain management. However, abuse and misuse of these drug products have created a serious and growing public health problem. One important step toward the goal of creating safer opioid analgesics has been the development of opioid drug products that are formulated to deter abuse. FDA considers the development of these products a high public health priority. It is important that generic versions of opioids that reference listed drugs whose labeling describes abuse-deterrent properties are available to help ensure availability of analgesics for patients who need them.

For FDA to approve an abbreviated new drug application (ANDA), the Agency must find, among other things, that the generic drug product has the same active ingredient(s), dosage form, route of administration, strength, and, with limited exceptions, labeling as the reference listed drug (RLD); is bioequivalent to its RLD; that the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are adequate to assure and preserve its identity, strength, quality, and purity; and that the inactive ingredients and composition of the generic drug are not unsafe for use under the conditions prescribed, recommended, or suggested in the labeling (see, e.g., the Federal Food, Drug, and Cosmetic Act (the FD&C Act) 505(j)(2)(A) and (j)(4) (21 U.S.C. 355(j)(2)(A) and (j)(4))). FDA classifies as "therapeutically equivalent" those products that meet the following general criteria: (1) They are approved as safe and effective; (2) they are pharmaceutical equivalents in that they: (a) Contain identical amounts of the same active ingredient in the same dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent; (4) they are adequately labeled; and (5) they are manufactured in compliance with current good manufacturing practices regulations. (See preface of Approved Drug Products with Therapeutic Equivalence Evaluations (commonly referred to as the Orange Book).) FDA believes that a product classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the reference product.

Accordingly, if the RLD's labeling describes abuse-deterrent properties, the ANDA applicant should evaluate its product to show that it is no less abuse-deterrent than the RLD with respect to all potential routes of abuse. Marketing a generic opioid drug product that is less

abuse-deterrent than the RLD could lead opioid abusers to preferentially seek out and abuse generics.

This draft guidance describes FDA's current thinking about the studies that should be conducted by a potential ANDA applicant and submitted to FDA in an ANDA to demonstrate that a generic solid oral opioid drug product is no less abuse-deterrent than its RLD with respect to all potential routes of abuse.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on the principles for evaluating the abuse-deterrence of generic solid oral opioid drug products. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

FDA intends to hold a public meeting following the close of the comment period to discuss further the evaluation of the abuse deterrence of generic opioid drug products and related issues, as appropriate. Further details will follow in a notice of public meeting published in the Federal Register.

II. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: March 21, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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